

Effects of cardiotrophin-1 on hemodynamics and endocrine function of the heart

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ABSTRACT: Cardiotrophin-1 (CT-1), a member of the interleukin-6 superfamily of cytokines, possesses hypertrophic actions and atrial natriuretic peptide (ANP)-producing activity in vitro. The goal of our study is to elucidate whether CT-1 affects the cardiovascular system in vivo. Intravenous injection of CT-1 (4-100 mug/kg) in conscious rats evoked significant declines in blood pressure and reflex increases in heart rate (HR) in a dose-dependent manner. CT-1 induced no significant change in cardiac output (from 260.7 +/- 11.0 to 264.7 +/- 26.6 mlcntdotmin-1cntdotkg-1, P = not significant), which was compatible with the results from isolated perfused rat hearts; HR, change in pressure over time, left ventricular developed pressure, and perfusion pressure were unaffected. Northern blot and RT-PCR analyses revealed that CT-1 increased expression of inducible nitric oxide synthase (iNOS) in lung and aorta but not in heart or liver. Pretreatment with aminoguanidine, a specific iNOS inhibitor, inhibited both iNOS mRNA production and the depressor effect of CT-1. Interestingly, CT-1 increased ventricular expression of ANP and brain natriuretic peptide (BNP). The data demonstrate that CT-1 elicits its hypotensive effect via a nitric oxide-dependent mechanism and that CT-1 induces ANP and BNP mRNA expression in vivo.

Postnatally induced inactivation of gp130 in mice results in neurological, cardiac, hematopoietic, immunological, hepatic, and pulmonary defects

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ABSTRACT: The pleiotrophic but overlapping functions of the cytokine family that includes interleukin (IL)-6, IL-11, leukemia inhibitory factor, oncostatin M, ciliary neurotrophic factor, and cardiotrophin 1 are mediated by the cytokine receptor subunit gp130 as the common signal transducer. Although mice lacking individual members of this family display only mild phenotypes, animals lacking gp130 are not viable. To assess the collective role of this cytokine family, we inducibly inactivated gp130 via Cre-loxP-mediated recombination in vivo. Such conditional mutant mice exhibited neurological, cardiac, hematopoietic,

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immunological, hepatic, and pulmonary defects, demonstrating the widespread importance of gp130-dependent cytokines.

In vivo effects of cardiotrophin-1

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ABSTRACT: Cardiotrophin-1 (CT-1) is a recently discovered cytokine that was isolated based on its ability to induce cardiac myocyte hypertrophy in vitro. In this study, the effects of chronic administration of CT-1 to mice (0.5 or 2 μ -g by intraperitoneal injection, twice a day for 14 days) were determined. A dose-dependent increase in both the heart weight and ventricular weight to body ratios was observed in the treated groups. The body weights of the animals were unaffected. These results indicate that CT-1 can induce cardiac hypertrophy in vivo. CT-1 was not specific for the heart, however. It stimulated the growth of the liver, kidney, and spleen, and caused atrophy of the thymus. CT-1 administration also increased the platelet counts by 70%, with no change in mean platelet volume. Red blood cell counts were increased in the treated animals, and there was a concomitant increase in haemoglobin concentration. Thus, CT-1 has a broad spectrum of biological activities in vivo. This observation is consistent with previous in-vitro findings showing that the mRNA for CT-1 is expressed in several tissues, and that CT-1 can function through binding to the leukaemia inhibitory factor (LIF) receptor and signalling through the gp130 pathway.

A new hepatocyte stimulating factor: Cardiotrophin-1 (CT-1)

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ABSTRACT: Recently, a novel cytokine, cardiotrophin-1 (CT-1), was cloned and found to induce cardiac myocyte hypertrophy in vitro. Amino acid sequence similarity showed CT-1 to be a member of the IL-6/LIF/CNTF/OSM/IL-11 cytokine family. Since all known members of the IL-6 cytokine family induce an hepatic acute phase protein (APP) gene expression, we investigated the ability of CT-1 to induce a liver acute phase response. Upon stimulation of rat hepatoma cells, CT-1 and LIF induced the strongest rat fibrinogen mRNA expression, OSM and IL-6 induced a less pronounced response. When human hepatoma cells and primary rat hepatocytes were stimulated with CT-1, the expression of human haptoglobin and rat alpha-2-macroglobulin mRNA was induced. The induction of the acute phase response was dose- and time-dependent. In this study we demonstrate that CT-1, a novel cytokine belonging to the IL-6 cytokine family, is a hepatocyte stimulating factor.

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Title: Cardiotrophin-1, the new member of the interleukin-6 cytokine

family. (ABSTRACT AVAILABLE)

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Abstract: Cardiotrophin-1 is a novel member of the interleukin-6 cytokine family. Mouse CT-1 mRNA is about 1.4 kb in length, and the encoded protein contains a 203-aa open reading frame. It utilizes gp130 and LIFR as the signal transducing receptor components. As a multi-functional cytokine, it induces cardiac myocyte hypertrophy and promote cardiac myocyte survival. It can induce a phenotypic switch in rat sympathetic neurons and promote the survival of dopaminergic neurons, ciliary neurons and motoneurons. It can also inhibit the growth of the mouse myeloid leukemia cell M1, and induce liver acute phase response. The chronic administration of CT-1 to mouse increases platelet counts, red blood cell counts and haemoglobin concentration.

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Murine cardiotrophin-1 stimulates the acute-phase response in rat hepatocytes and H35 hepatoma cells

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Set	Items	Description
S1	2066	CARDIOTROPHIN
S2	129	S1 (S) (LIVER OR HEPATIC)
S3	86	S2 NOT PY>2002
S4	17	RD (unique items)